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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/456,693	12/09/1999	DASA LIPOVSEK	COTH-P01-507	6778

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/456,693	LIPOVSEK, DASA	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8,9 and 11-52* is/are pending in the application.

4a) Of the above claim(s) *13-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8,9,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/25/04 has been entered.

Status of Claims

Claims 1 and 8-9 and 11-52 are pending in the application.

Claims 2-7 and 10 have been cancelled.

Claims 13-52 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 1, 8, 9, 11 and 12 are under examination.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 8, 9, 11 and 12 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility for reasons set forth in the last Office action.

Response to Arguments

Applicants incorporate the Response filed September 12, 2003 and briefly reiterate and argue that the library provides specific and substantial utility. Applicants argue that the subject libraries are, in fact, novel collections of proteins that are particularly suitable for at least one purpose, such as the identification of proteins that bind to a selected target. One could not reasonably screen all of nature to identify, for example, TNf-alpha binding agents. Nor could one reasonably screen almost any other library of proteins (excepting, perhaps, antibody libraries) and expect to identify such binding agents. The mere fact that a library as a whole will not be useful for treating, e.g., inflammation, does not mean the library is useless. Likewise, the mere fact that the library contains component parts that are individually useful for therapeutic purposes should not negative the usefulness of the library as a whole for finding such useful components.

In response, the reply to the September 12, 2003 is also hereby incorporated. The alleged novel collections of proteins

are nothing more than those occurring naturally which in and of itself will naturally bind to its natural target. As stated by applicants above, screening are specifically drawn to those samples that are suspected or known to contain the fibronectin molecule and not a shot in the dark screening of the entire nature's source. The utility of a library or each of the components therein does not have to be useful for therapeutic purposes to have a utility. Rather, that the library must have a ***specific and substantial*** utility or evidentiary support for the asserted utility. Said utility does not have to be a therapeutic utility, as argued. It is of interest to note, that the specification has not identified any compounds that have been isolated from the library that has binding effect or utility. Furthermore, the claimed library would read on naturally occurring collection of molecule, which is therefore not a novel library (i.e., simply nature's collection of compounds.)

Applicants remind the Examiner that screening assays or other methods for identifying compounds that themselves have therapeutic activity are widely patentable.

In reply, the claims are drawn to library and not screening assays.

Applicants urge that in Brenner, the claimed subject màtter was a method for generating a compound with no known use. Brenner at 383 U.S. 519 at 532 (1966). The presently claimed libraries are compositions of matter that, for example, allow one of ordinary skill in the art to generate compounds with real uses, such as compounds that bind and inhibit TNF-alpha.

In response, as stated by applicants it is the compounds in the library that bind and inhibit TNF-alpha i.e., the one that has a specific and substantial utility. Brenner is cited not for the specific compound not having the utility. Rather, it was cited for the expressed opinion of the court that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility….A patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion. "Congress intended that no patent be granted on a chemical compound whose sole

'utility' consists of its potential role as an object of use-testing." (Emphasis added). See also University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003). There is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

Applicants draw the Examiner's attention to the fact that numerous U.S. patents have issued that claim libraries of peptides. And many companies have been built based on their novel or proprietary libraries of useful compounds including peptides and mimetics (including antibodies), nucleic acids, small molecules, etc. Clearly, a library of useful compounds can lead to not only discoveries that confer clinical benefits but also successful business platforms.

In response, each case is treated on its own merits. Furthermore, the commercial success of a compound does not necessarily follow that it has a specific and substantial utility as required by the statute.

Claims 1, 8, 9, 11 and 12 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled

in the art clearly would not know how to use the claimed invention.

The response above is incorporated herein since applicants incorporated their arguments above.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 8-12, as amended, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Response to Arguments

In view of the cancellation of claim 10, the written description in the last Office action is withdrawn.

Claim 1, as amended, does not provide support for the presently claimed "plurality of fibronectin-based scaffolds having a fibronectin type III domain in which at least three

solvent accessible loops are randomized." The as-filed specification does not recite for a plurality of fibronectin-based scaffold that with at least three loops are solvent accessible. Applicants point out support for the amendment at page 7, line 12 for the term fibronectin type 111 domain.

In response, the cited relevant page does not define a plurality for said library nor the loops as being accessible. Rather, as stated by applicants it defines only the term fibronectin type III domain. The as-filed specification recites for a solvent exposed, which is not the same as solvent accessible. Webster's dictionary defines accessible as easily entered or approached. Exposed is defined as to lay open or make visible.

The specification fails to describe a library of proteins that comprise a plurality of fibronectin-based scaffolds. Said scaffolds have a fibronectin type III domain with the ability to bind compounds that are not bound by a human fibronectin type III domain. It is not apparent from the disclosure as to the number included in the term plurality or the manner by which a scaffold is fibronectin-**based.** This is made more complex as the claims do not recite for any structure or formula of said fibronectin-based scaffold. A "written description of an invention involving a chemical genus, like a description of a

chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 as amended, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

A. Claim 8 is unclear as to the manner the length is extended "corresponding" to the human Fn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 8, 9 and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Koide [2002/0019517 which is the same as (U.S. 6,462,189] for the same reasons set forth in the last Office action.

Response to Arguments

Applicants argue that although Koide teaches more than one variegation within one loop, it never teaches three randomized loops. Examples IV and V of Koide describes loop variegation in only one of the five loops. But admit that the example in Koide where more than one loop were variegated or randomized is Example VI. Koide teaches variegations introduced to both FG and BC loops. Applicants argue that at most, Koide teaches a monobody with two variegated loops (BC and FG) and maybe additional mutations in the N-terminal tail, not in any of the other three loops. Koide also teaches away from randomizing another loop in addition to the BC and FG loops, because the other loops have better defined structure than the N-terminal tail and would be expected by Koide as contributing to the

stability of the monobodies. Therefore, Koide does not expressly or inherently teach the element of "at least three randomized loops" and does not anticipate the instant claimed invention.

In response, applicants not only admit above, and also in the September reply, that paragraphs 0022-0028(page 2) of Koide state that one or more of the monobody loop regions sequences of the Fn3 polypeptide vary by deletion, insertion or replacement. This paragraph also lists which amino acids make up the AB, BC, CD, DE, EF and FG loops. Attention is further drawn to Examples IV and V, page 12, which recites at least 3 randomization of the loops. Koide, specifically recites the at least three (i.e., five) of the specific loop positions that can be randomized.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 8, 9, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koide.

Response to Arguments

Applicants argue that Koide teaches away from making Fn-based monobodies having more than two randomized loops and does not provide a reasonable expectation of success to modify its monobodies (e.g., to variegate a third loop in addition to the BC and FG loops) to achieve the present invention.

In reply, applicants' attention is drawn to Example V wherein Koide discloses randomization in the BC and FG loop and other variegation in the other loops such as the CD, DE or EF loop. These loops are defined at page 4, lines 25-45. Applicants cannot pick and choose the prior art teaching ignoring the totality of its teaching. Koide is not a teaching away. Rather, provides guidance as to which loop modifications have to be avoided that would result in the instability of the fibronectin scaffold.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0812. The fax phone number for the

organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
June 25, 2004